Results from a Mailed Promotion of Medication Reviews Among Department of Defense Beneficiaries Receiving 10 or More Chronic Medications

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ABSTRACT

BACKGROUND: Like many payers, the Department of Defense (DoD) has limited ability to work directly with prescribers to ensure appropriate medication use. Many older beneficiaries are prescribed multiple maintenance medications, placing them at higher risk for adverse drug interactions, contraindicated medication use, and other polypharmacy-related problems. Medication reviews may mitigate these risks, but the optimal venue for medication therapy management is unclear.

OBJECTIVES: To (a) determine if beneficiaries will respond to a mailed request from the DoD to pursue a medication review; (b) identify medication review location and outcomes from the patient perspective; and (c) assess the statistical significance of changes in the number of prescription medications overall and for key categories, including maintenance medications and contraindicated medications, relative to a propensity-matched comparison group.

METHODS: A total of 4,000 TRICARE beneficiaries aged 55 years or older, residing in North Carolina, who obtained 10 or more maintenance medications (defined by a unique combination of drug, strength, and dosage form) during the 90-day baseline period from May 3, 2008, to July 31, 2008, were mailed letters requesting their participation in the study. Consenting subjects received a personalized medication list to review with their physicians or pharmacists and a survey form to complete after the review. Survey results were compared by location of medication review (i.e., physician's office, pharmacy, or both). Changes from the 90-day baseline to 90-day post-intervention period were calculated for prescription utilization measures (total drug count, maintenance drug count, count of Beers list medications, and count of contraindicated drug combinations) for the subsample of subjects who completed the survey ($n=373$) and for subjects who received the initial consent letter ($n=3,856$) versus a propensity-matched comparison sample drawn from neighboring states. Variables included in the propensity score were gender, age group, military rank, catchment status indicating proximity to military pharmacies, enrollment status, number of pharmacy settings used, and each of 30 binary disease indicators.

RESULTS: A total of 1,469 subjects responded to the consent letter (response rate=38.1%); 606 subjects consented to participate (consent rate=15.7%); and 373 subjects returned a completed survey (completion rate=9.7%). Among those who completed the survey, 190 (50.9%) received reviews in a physician's office; 103 (27.6%) received reviews in a pharmacy; 60 (16.1%) received reviews in both locations; and 20 (5.4%) reported a different location or no location. 61 survey respondents (16.4%) indicated that they were told to stop a medication, and 77 (20.6%) reported a dosage change. Medication changes occurred significantly more frequently for reviews performed at a physician's office compared with other review locations. Therapeutic classes most frequently stopped or adjusted for dosage were antidiabetics, diuretics, antilipidemics, renin-angiotensin aldosterone system inhibitors, anticoagulants, nonsteroidal anti-inflammatory drugs,

and beta-adrenergic blocking agents. 85% of respondents reported that the medication review was worth doing. In the assessments of changes in prescription utilization from the baseline to post-intervention periods, no significant by-group differences were noted among those who completed the study relative to their matched comparison subjects. In the comparison of subjects who received the initial consent letter with their matched counterparts, small but statistically significant differences were observed for several prescription utilization measures, including changes in use of high-risk Beers list medications ($P=0.033$); use of electrolytic, caloric, and water balance medications ($P=0.038$); and use of hypertension medications ($P=0.028$). The magnitude of the decrease observed among comparison subjects, however, exceeded that observed among the case subjects.

CONCLUSIONS: Response was poor to a mailing that promoted a beneficiary-initiated medication review. The absence of significant changes following the medication review suggests several possibilities: a mailed intervention is ineffective in promoting medication review; medication regimens for study subjects are already optimized to the extent obtainable through a routine medication review; or the study sample size was too small to detect relevant changes. Most drug regimen changes were dosage adjustments for current medications or substitutions within the same therapeutic class. The extent to which comprehensive assessment of a patient's medication regimen, including nonprescription and herbal agents, was performed is unclear. More intensive interventions may be required to ensure that medication regimens are being actively managed among those who use a large number of prescription medications.

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What is already known about this subject

- Interventions that involve collaboration among patients, physicians, and/or pharmacists have been significantly associated with improvements in medication adherence, persistence, and attainment of clinical goals for specific disease states, as well as reductions in the number of medications or the number of high-risk drugs or drug combinations in a patient's regimen.
- The 2009 National Committee for Quality Assurance physician metric for medication review among older adults specifies that "counseling about medication" be performed but does not provide guidance about how counseling should be performed, and no clear consensus has emerged regarding the best tools and methods for conducting reviews.

What this study adds

- A mailed letter promoting beneficiary-initiated medication reviews among patients with high polypharmacy-related risks is not an effective means of ensuring receipt of comprehensive medication reviews.
- When given the choice to seek a medication review with their physicians, pharmacists, or toll-free pharmacy call center, 51% of patients sought reviews at the physician's office. Approximately one-half of those patients reported that their medication reviews were performed without a specific request from the patient, family member, or caregiver.
- Routine medication reviews, although viewed positively by most patients, are not associated with significant changes in the total number of medications used, number of maintenance medications used, use of contraindicated drug pairs, or use of Beers list medications (drugs inappropriate for prescribing among the elderly).
- Among the 7.2% of the study sample members who had 1 or more severity level 1 drug-drug interaction (DDI) in their medication list, more than 70% of the medication pairs included oral, solid formulations of potassium chloride. This finding suggests the potential for alert fatigue and the need to refine the electronic alert system to generate alerts for only those drug pairs that pose the greatest risk to patient safety.

Polypharmacy, generally defined as the simultaneous use of multiple medications, has been repeatedly identified as an area of concern, particularly among older patients.¹ Although older patients typically require a combination of medications to manage multiple comorbidities, no clear rule of thumb has emerged regarding the number of medications that may be safely used concomitantly. However, there is compelling evidence that the potential for adverse drug-related events, including drug-drug interactions, drug-nondrug interactions, drug-disease interactions, adverse side effects, and medication nonadherence, increases with the number of medications being used. Many of these events may be preventable.²⁻⁴ Often, a critical review of an individual's medication usage is not conducted until after an adverse drug-related event occurs.⁵ The literature suggests that the most effective interventions for mitigating polypharmacy-related risk involve active collaboration among patients, physicians, and pharmacists.⁶⁻⁸ The extent to which this type of collaboration occurs outside the scope of a study or program specifically designed to promote it is unclear.

In 2007, the Department of Defense (DoD) TRICARE Management Activity determined that 13% of its beneficiaries aged 65 years or older were using in excess of 10 different medications simultaneously.⁹ Although the vast majority of older beneficiaries use the TRICARE pharmacy benefit, with

its low copayments and broad array of formulary medications,¹⁰ relatively few enroll in TRICARE Prime, the DoD's managed care plan. Instead, many military retirees and their dependents use Medicare or other civilian health plans (with TRICARE as a second payer) to obtain some or all of their health care services. This arrangement limits the DoD's ability to work directly with prescribers to ensure that beneficiaries' medication usage is being appropriately monitored. Because the DoD, like many payers, has limited ability to work directly with prescribers, interventions targeting beneficiaries and their pharmacists are the primary means of promoting safe and effective medication use.

DoD already provides the dispensing pharmacist with the ability to conduct a prospective drug utilization review (PDUR) on each new and refilled prescription using the beneficiary's complete TRICARE drug profile. However, the extent to which a PDUR can identify all polypharmacy-related risks is unclear.¹¹ Most PDUR programs lack patient-specific, clinical information necessary to identify inappropriate prescribing, and pharmacists' responses to an alert may vary depending on their workload or information available at the time of dispensing. PDUR will detect only drug-drug interactions (DDIs) or therapy dosage or duration problems that have been programmed into the software, which requires regular updates.¹² Additionally, even the most current PDUR program cannot identify pharmacotherapy problems associated with diet, lifestyle, over-the-counter (OTC) medication use, and barriers associated with patient adherence with critical medications.

Thus, the DoD elected to undertake a pilot study that would encourage beneficiaries aged 55 years or older with the highest prescription medication usage to actively pursue a full medication review. The Polypharmacy Intervention Pilot (PIP) study was initiated in 2008 with the following objectives: (a) determine if beneficiaries will obtain a medication review if asked to do so in a letter sent from the DoD; (b) describe where beneficiaries go to obtain a medication review and their perceptions of what occurred during the review; and (c) assess the statistical significance of post-intervention changes in medication utilization relative to those of a propensity-matched comparison group. Because clinical and medical claims data were not available for most beneficiaries, prescription drug utilization measures were used to assess outcomes. Specific measures included the number of prescription medications in total, for maintenance medications, and for medications associated with specific therapeutic classes and disease states; the frequency of contraindicated drug combinations; and the prevalence of Beers list medications contraindicated for use in the elderly, calculated for the subset of sample patients who were aged 65 years or older. The present study report describes the PIP initiative, results from its implementation, and implications for policymakers and future studies.

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Methods

Sample Selection

The study focused on TRICARE beneficiaries in North Carolina (NC), which has a high volume of older TRICARE beneficiaries who reside in approximately equal numbers inside and outside the catchment area of a military medical facility. Catchment areas are defined as the 40-mile, ZIP code-based radius of a military hospital (housing a large military pharmacy) or a 20-mile, ZIP code-based radius of a military clinic (housing a smaller military pharmacy). Residential catchment status is considered important to control for potential effects of out-of-pocket prescription drug costs; beneficiaries living near a military facility may be more likely to use military pharmacies, which offer TRICARE beneficiaries up to a 90-day supply of medication at \$0 copayment. TRICARE beneficiaries pay \$3, \$9, or \$22 (based on a 3-tier formulary structure) for up to a 30-day supply at community pharmacies or up to a 90-day supply in the DoD mail order program.

Outpatient prescription fill records were used to identify potential study subjects (Figure 1). All prescriptions filled under the TRICARE pharmacy benefit at any military or network community pharmacy or the DoD mail order pharmacy are processed through the DoD's Pharmacy Data Transaction Service (PDTs). PDTs performs a PDUR against the beneficiary's complete DoD drug profile. All completed prescription fill records are then forwarded to a central data repository where data are processed and made available for operational and research use. Outpatient prescription fill records for NC residents aged 55 years or older for a 90-day baseline period from May 3, 2008, to July 31, 2008, were analyzed. The 4,000 NC residents taking 10 or more maintenance medications, defined by unique combination of drug, strength, and dosage form according to the First DataBank (San Francisco, CA) generic code number (GCN) and maintenance medication indicator, were identified as target subjects. The address of record was verified using the National Change of Address process through the U.S. Postal Service. Subjects whose mail address could not be verified (approximately 1%) were excluded from the study. The choice of a 10-medication threshold was based on budgetary constraints for the pilot that did not permit targeting a larger population. A group of 19,642 potential comparison subjects was also selected from among the residents of Georgia, South Carolina, and Virginia, using the same criteria. Three states were needed for selection of comparison subjects because no one state had sufficient numbers of older DoD beneficiaries to support construction of a suitable comparison group.

Intervention Procedures

The PIP intervention package consisted of a letter requesting that subjects pursue a medication review and a personalized medication list designed to facilitate the review process. Human subject research guidelines required written consent of

each subject's participation because protected health information would be included in the PIP intervention package. During the week of September 2, 2008, consent letters describing the study were mailed to the 4,000 target subjects. Because institutionalized persons or those receiving end-of-life care were unlikely to benefit from participation, the instructions directed these individuals to return their consent form, indicating that they declined participation for one of those reasons. As of January 31, 2009, the last date that signed consent letters were accepted, 144 letters were returned as nondeliverable, and 1,469 of the remaining 3,856 subjects responded to the consent letter for a response rate of 38.1%. A total of 606 (15.7%) subjects consented to participate, 404 (10.5%) subjects declined on the basis of having recently had a medication review, and 459 (11.9%) subjects declined for other or no reason given. No financial incentives or reimbursements for participation were offered, and no second mailing or replacement sampling was attempted.

Consenting subjects were mailed the study package containing a medication list and a short survey form during the week of September 2, 2008. The medication list included the generic and brand names and last fill dates for each medication obtained during the baseline period. Subjects were asked to validate the list of medications and add missing prescriptions, OTC products, and herbal remedies used. They were then instructed to have the list reviewed by their pharmacist or primary care physician during their next scheduled appointment. The letter also indicated that DoD mail order pharmacy users could request their medication review by telephone using a dedicated, toll-free number. Military pharmacies, DoD mail order personnel, and community pharmacies in the TRICARE network were notified of the PIP study procedures in advance, but no reimbursements or financial incentives were offered for performing drug reviews for PIP participants.

A follow-up telephone call was made to subjects who did not return the survey within 60 days. If the medication review had already occurred but the survey was not yet returned, the subject was given the option of completing the survey by telephone. Receipt of survey response, either written or verbal, completed the subject's participation in the study. A total of 373 subjects (9.7%) completed the study. Of the remaining 233 initially consenting subjects, 120 actively withdrew from the study, most citing poor health as the reason. The remaining 113, for unknown reasons, did not return the survey at any time during or after the close of the fielding period on March 31, 2009. This study was approved by the U.S. Army Medical Research and Materiel Command Office of Research Protections on May 14, 2008.

Data Analysis

PIP subjects were analyzed as 2 groups. The first group comprised all study subjects ($n=3,856$), and the second group

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FIGURE 1 Polypharmacy Intervention Pilot Case Subject Selection

^aPrior to selection of the target population, addresses of potential subjects were verified using the National Change of Address process through the U.S. Postal Service. Potential subjects without a valid address were excluded.

^bAll rates were calculated as a percentage of the total study sample of beneficiaries who received consent letters (n=3,856).

NC=North Carolina.

comprised those who completed the study (n=373). For the latter group, survey results were compiled and compared by location of the medication review: a physician's office, a pharmacy, both, or neither.

To quantitatively assess the impact of the intervention, an

analysis was conducted to compare prescription utilization in each study group before and after the intervention relative to that observed for a propensity-matched comparison group. Propensity scores are commonly used to select suitable comparison subjects in studies with observational designs.¹³ To

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FIGURE 2 Polypharmacy Intervention Pilot Case and Comparison Groups

^aAfter the comparison group was initially developed, the case and comparison groups were monitored independently throughout the post-intervention period. For example, if a case subject died or was otherwise dropped from the study, no effort was made to remove the matched comparison subject.

^bThe post-intervention period was 90 days in length for all subjects. The start date of the post-intervention period was the survey return date for subjects who completed the study or December 1, 2008, for all other subjects.

Rx=prescription.

calculate a propensity score for each subject, all 3,856 case subjects and 19,642 potential comparison group subjects were included in a logistic regression model in which the binary dependent variable was NC residential status (i.e., NC residents were assigned “1” and nonresidents were assigned “0”).¹⁴ The predicted probability for each subject in the regression model was saved as the subject’s propensity score.

The variables included in the regression model included gender, age group (55 to 64 years, 65 to 74 years, 75 years or older), rank (enlisted, officer), catchment status (in-catchment, noncatchment), enrollment status (TRICARE-enrolled, not enrolled), number of pharmacy settings used during the baseline period (1, 2, or more), and each of 30 binary disease indicators. Income and educational level data were not available. The rank of the active or retired military service member was used as a proxy for socioeconomic status. (In general, military officers are more likely to be college-educated and draw a larger salary or retirement pay than their enlisted counterparts.) The values for pay grade were dichotomized into officer (includes active and retired officers and their family members) and enlisted (includes active and retired enlisted personnel and

their family members). The number of pharmacy settings used was included in the propensity score calculation due to a prior study finding that patients who take multiple medications are skilled at using multiple pharmacy settings (military, community, or mail order) to minimize out-of-pocket costs.¹⁵ The 30 binary disease indicators were coded using the methodology described by Clark et al. (1995).¹⁶ Each case and potential comparison subject was assigned a 1 or 0 for a specific disease, based on the presence or absence of a maintenance medication for that condition in his or her baseline medication list. Each of these indicators was subsequently entered as a variable in the regression model. The c-statistic (area under the receiver operating characteristic [ROC] curve) assessing the predictive accuracy of the probabilities estimated by the regression model for the 3,856 case subjects and the 19,642 potential comparison group subjects was 0.585.

Before propensity-score matching each case subject with a comparison subject, all subjects were assigned to 1 of 24 cells, each defined by a unique combination of age group, gender, sponsor rank, and catchment status. This step was performed to ensure an exact match on these demographic variables for

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TABLE 1 2003 Beers List Medications Considered Potentially Inappropriate for Treatment of the Elderly, Independent of Dosage, Diagnosis, or Disease State

Medications Rated as High Severity^a

amiodarone; amitriptyline; amphetamines (excluding methylphenidate HCl and anorexics); amphetamines and anorexic agents; anticholinergics and antihistamines; barbiturates (except phenobarbital); chlorpropamide; daily fluoxetine; desiccated thyroid; diphenhydramine; disopyramide; doxepin; flurazepam; gastrointestinal antispasmodic drugs; guanadrel; guanethidine; indomethacin; ketorolac; long-term use of full-dosage, longer half-life, non-COX selective NSAIDs; long-term use of stimulant laxatives; long-acting benzodiazepines; meperidine; meprobamate; mesoridazine; methyl dopa; methyltestosterone; mineral oil; muscle relaxants and antispasmodics; nitrofurantoin; orphenadrine; pentazocine; propoxyphene napsylate/acetaminophen; short-acting nifedipine; thioridazine; ticlopidine; trimethobenzamide.

Medications Rated as Low Severity^a

clonidine; cimetidine; cyclandelate; digoxin; doxazosin; ergot mesyloids; estrogens only (oral); ethacrynic acid; isoxsuprine; propoxyphene; short-acting dipyridamole.

^aFick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults (2003).¹⁷ COX=cyclooxygenase; HCl=hydrochloride; NSAID=nonsteroidal anti-inflammatory drug.

each case-comparison pair. Within each cell, case subjects were then matched one-to-one with a comparison subject based on similar propensity scores. If multiple potential comparison group subjects had a match on the propensity score, 1 was selected at random.¹⁴ A total of 61.2% of case-comparison pairs had an exact match on the 5-digit propensity score (e.g., 0.12345), and 36.9% of cases were matched with comparison subjects whose scores differed by less than 10.0%. The remaining 1.9% of cases had scores that differed by more than 10% relative to their matched comparison subject. The final c-statistic comparing the predicted probabilities estimated by the regression model for the 3,856 case subjects and the 3,856 comparison subjects was 0.503. A c-statistic value of 0.5 indicates a randomized distribution of case and comparison subjects, which suggests that our matching methodology produced a comparison group nearly identical to our case group insofar as the regression model would allow.

By-group comparisons of changes in prescription utilization from the 90-day baseline period to the 90-day post-intervention period were performed. The index date for the start of the post-intervention period varied by subject. For case subjects who completed the study, the index date was the date on which their survey package was returned rather than the medication review date because only the month and year of the review date were requested on the survey form. For all other case subjects, the index date was December 1, 2008. Prescription utilization for each comparison subject was assessed using the same post-intervention period assigned to his or her matched case.

Once the index date was assigned to each case and comparison subject, the case and comparison groups were treated independently. Using available TRICARE claims data, we determined that a total of 607 case subjects and 596 comparison subjects were known to have died, been hospitalized, or failed to fill any prescriptions under the TRICARE drug benefit during the post-intervention period. These individuals were excluded from the utilization analyses, but their surviving, matched subjects were retained (Figure 2).

By-group differences in mean changes in prescription utilization were assessed using the 2-sided t test. Measures of prescription utilization included the number of prescription medications; maintenance medications; Beers list medications classified as high- or low-risk medications contraindicated for patients aged 65 years or older, independent of diagnosis, condition, or dosage, revised as of 2003 (Table 1);¹⁷ severity level 1 DDI pairs (contraindicated drug combinations) as defined by First DataBank (San Francisco, CA); medications classified by American Hospital Formulary Service (AHFS) therapeutic category; and medications for each of 30 disease categories.

SAS version 9.1 (SAS Institute Inc., Carey, NC) was used for dataset extraction and propensity-score matching. SPSS version 17.0 (SPSS Inc., Chicago, IL) was used for statistical analyses. Because we elected to treat the case and comparison groups independently, statistical significance of the mean change in prescription utilization pre- and post-intervention was assessed using the 2-sided t-test for independent groups, rather than using the t-test for matched pairs. Although this approach reduced our statistical power for between-group comparisons, it allowed for inclusion of utilization data for unmatched subjects in our calculations. The a priori threshold for statistical significance was $P < 0.05$.

Results

Table 2 presents a description of NC case subjects, the comparison subject groups before and after propensity matching, and case subjects who completed the study. Subgroups that were predominant among study cases included females (57.3%), patients aged 65 to 74 years (43.4%), enlisted service members and dependents (80.5%), nonenrolled subjects (80.5%), and catchment residents (54.4%). Prior to propensity matching, statistically significant differences across all variables examined, except gender, were observed between the NC case subjects and the potential comparison subjects from surrounding states. After propensity matching, the case group retained a significantly higher proportion of TRICARE

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TABLE 2 Demographic Characteristics and Baseline Utilization: Case and Comparison Subjects, Before and After Propensity-Score Matching, and Case Subjects Who Completed the Study

	Case Subjects		Propensity-Matched Comparison Subjects				Case Subjects Completing Study			
			Before Matching		After Matching					
	n	(%)	n	(%)	P Value ^a	n	(%)	P Value ^a	n	(%)
Total	3,856	(100.0)	19,642	(100.0)		3,856	(100.0)		373	(100.0)
Gender ^b					0.805			1.000		
Male	1,646	(42.7)	8,343	(42.5)		1,646	(42.7)		202	(54.2)
Female	2,210	(57.3)	11,299	(57.5)		2,210	(57.3)		171	(45.8)
Age group ^b - years					<0.001			1.000		
55 to 64	932	(24.2)	4,470	(22.8)		932	(24.2)		83	(22.2)
65 to 74	1,675	(43.4)	7,850	(40.0)		1,675	(43.4)		180	(48.3)
75 or older	1,249	(32.4)	7,322	(37.3)		1,249	(32.4)		110	(29.5)
Rank ^b					<0.001			1.000		
Enlisted and dependents	3,104	(80.5)	14,057	(71.6)		3,104	(80.5)		283	(75.9)
Officers and dependents	752	(19.5)	5,585	(28.4)		752	(19.5)		90	(24.1)
TRICARE enrollment					0.010			<0.001		
Enrolled	753	(19.5)	4,197	(21.4)		617	(16.0)		94	(25.2)
Not Enrolled	3,103	(80.5)	15,445	(78.6)		3,239	(84.0)		279	(74.8)
Catchment status ^b					0.002			1.000		
In catchment	2,097	(54.4)	10,153	(51.7)		2,097	(54.4)		193	(51.7)
Noncatchment	1,759	(45.6)	9,489	(48.3)		1,759	(45.6)		180	(48.3)
Pharmacy settings used ^c					0.048			0.057		
1 setting only	1,728	(44.8)	9,144	(46.6)		1,645	(42.7)		122	(32.7)
Multiple settings	2,128	(55.2)	10,498	(53.4)		2,211	(57.3)		251	(67.3)
Mean [SD] number of medications ^d										
Total prescription medications	15.41	[3.65]	14.92	[3.70]	<0.001	14.89	[3.75]	<0.001	14.86	[3.30]
Maintenance medications	12.41	[2.06]	11.92	[2.07]	<0.001	11.88	[2.02]	<0.001	12.29	[2.00]
Beers list users ^e										
High-risk medication	1,053	(36.0)	5,431	(35.8)	0.823	1,104	(37.8)	0.167	94	(32.4)
Low-risk medication	1,058	(36.2)	5,319	(35.1)	0.243	1,049	(35.9)	0.806	91	(31.4)
Severity level 1 DDI ^f										
1 or more DDI	280	(7.3)	1,218	(6.2)	<0.001	222	(5.8)	0.007	31	(8.3)
C-statistic			0.585			0.503				

^aStatistical significance was assessed using Pearson chi-square for categorical variables and 2-sided t-test for continuous variables.

^bDenotes a variable that was used to perform propensity-score matching between case and comparison subjects.

^cSettings include military pharmacies, community pharmacies, and the TRICARE mail order pharmacy.

^dA prescription medication was defined by 1 or more fills for a unique GCN during the 90-day baseline period.

^eOnly subjects aged 65 years or older (n=2,924 study cases, of whom 290 completed the study; n=15,172 potential comparison group subjects, of whom 2,924 were matched to case subjects) were assessed for presence of 1 or more Beers list medications in their baseline medication lists.

^fDefinition of DDI: subject obtained 2 medications during the baseline period that constitute a contraindicated drug combination.

DDI=drug-drug interaction; GCN=generic code number; SD=standard deviation.

enrollees (19.5% and 16.0% for case and comparison groups, respectively); a higher mean [SD] number of total medications (15.41 [3.65] and 14.89 [3.75], respectively) and maintenance medications (12.41 [2.06] and 11.88 [2.02], respectively); and significantly more subjects with 1 or more DDI pairs in their medication lists (7.3% and 5.8%, respectively). Among the case subjects, higher proportions of males (54.2%), patients aged 65 to 74 years (48.3%), officers and dependents (24.1%), TRICARE enrollees (25.2%), and users of multiple pharmacy settings (67.3%) completed the study.

Of subjects aged 65 years or older, approximately one-third

of cases had 1 or more Beers list medications, and 6%-8% had 1 or more severity level 1 DDI pairs in their baseline medication lists. The most frequently observed high-risk Beers list medications were amitriptyline, promethazine, cyclobenzaprine, amiodarone hydrochloride (HCl), fluoxetine, oxybutynin, and diazepam. Most frequently observed low-risk medications were digoxin, propoxyphene/acetaminophen, clonidine HCl, conjugated estrogens, and doxazosin mesylate. Approximately 71% of all potential DDIs comprised medications contraindicated for use with oral, solid formulations of potassium chloride. The observed contraindicated drug-drug

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TABLE 3 Severity Level 1 DDI Pairs^a

Drug #1	Drug #2	Number of Patients	Percentage of DDIs ^b	Commonly Indicated Condition
KCl	Tolterodine tartrate	112	18.1	Overactive bladder
KCl	Oxybutynin/oxybutynin chloride ^c	67	10.8	Overactive bladder
KCl	Diphenoxylate hydrochloride/atropine sulfate	43	7.0	Diarrhea
KCl	Darifenacin hydrobromide	40	6.5	Overactive bladder
KCl	Dicyclomine hydrochloride ^c	36	5.8	Irritable bowel syndrome
KCl	Solifenacin succinate	35	5.7	Overactive bladder
KCl	Hysocyamine sulfate ^c	21	3.4	Peptic ulcer disease
KCl	Hydrocodone bit/homatropine	16	2.6	Symptomatic relief of cough
KCl	Trospium chloride	15	2.4	Overactive bladder
KCl	Benzotropine mesylate	8	1.3	Parkinsonian syndrome
KCl	Scopolamine hydrobromide	8	1.3	Antiemetic
KCl	Chlordiazepoxide/clidinium bromide ^c	6	1.0	Peptic ulcer disease
KCl	Glycopyrrolate	6	1.0	Peptic ulcer disease
KCl	Phenylephrine/chlor-mal/scop	6	1.0	Nasal congestion
KCl	Trihexyphenidyl hydrochloride	5	0.8	Parkinsonian syndrome
KCl with other contraindicated drugs (n<5)		16	2.6	
Total (KCl)		440	71.2	
Nitroglycerin	Vardenafil HCl	9	1.5	Erectile dysfunction
Nitroglycerin	Sildenafil citrate	6	1.0	Erectile dysfunction
Nitroglycerin	Tadalafil	1	0.2	Erectile dysfunction
Total (nitroglycerin)		16	2.6	
Other contraindicated drug pairs (n<5)		162	26.2	
Total (all contraindicated drug pairs)		618	100.0	

^aIdentified in the medication lists for case subjects during the baseline period. Listed in order of descending frequency of subjects using the DDI pair. Numbers sum to more than 373 because some subjects had more than 1 interacting pair.

^bCalculated as a percentage of the total count of DDIs.

^cHigh-risk Beer's list medication.

DDI=drug-drug interaction; HCl=hydrochloride; KCl=potassium chloride.

combinations are displayed in Table 3.

PIP survey responses by review location are presented in Table 4. Respondents were asked to indicate the location of their reviews rather than identify the type of provider who performed the review to prevent them from making assumptions about who may be involved in the review process. A total of 190 (50.9%) received reviews in a physician's office; 103 (27.6%) received reviews in a pharmacy; and 60 (16.1%) received reviews in both locations, while 20 (5.4%) received reviews elsewhere or did not answer the question. A total of 142 (38.1%) respondents reported that a medication review was performed without a specific request from the patient, a family member, or caregiver. Respondents whose review involved a physician's office visit were significantly more likely to report a review without request (52.1% for physician's office alone, 41.7% for physician's office and a pharmacy) relative to those who received reviews at a pharmacy alone (9.7%, $P=0.002$).

A total of 61 respondents (16.4%) indicated that they were told to stop using 1 or more medications, and 77 (20.6%) reported that they were told to change a dosage for an existing medication. Reports of both medication changes and dosage changes occurred at 2 to 3 times the rate among cases whose

review locations included a physician's office, compared with those who received pharmacy-only reviews ($P=0.024$ and $P<0.001$, respectively). Medications most frequently reported as stopped were in the therapeutic classes of antidiabetics ($n=12$), antilipidemics ($n=7$), renin-angiotensin aldosterone system inhibitors ($n=7$), and nonsteroidal anti-inflammatory drugs (NSAIDs, $n=7$). Those most frequently reported as dose-adjusted were antidiabetics ($n=15$), diuretics ($n=10$), anti-coagulants ($n=7$), antilipidemics ($n=7$), and beta-adrenergic blocking agents ($n=6$).

A total of 23 (6.2%) respondents reported being told to stop using an OTC or herbal medication, and the medications mentioned were NSAIDs ($n=13$), vitamins ($n=7$), calcium ($n=2$), potassium ($n=1$), omeprazole ($n=1$), and glucosamine ($n=1$). A total of 105 (28.2%) respondents reported being counseled to avoid certain foods or drinks when taking their medications; 56 (15.0%) were told that 1 or more of their medications were available at lower cost; and 22 (5.9%) reported that during the medication review, their provider learned about 1 or more medications "that he or she did not know you were taking." No significant differences were observed for these 4 measures across review locations. Finally, 85%-90% of respondents

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TABLE 4 Survey Results for Case Subjects Who Completed the PIP by Medication Review Location

n (%)	Total	Physician's Office	Pharmacy ^a	Physician's Office and Pharmacy ^b	Other ^c or No Response	P Value ^d	Response Detail
Survey Response	n = 373	n = 190	n = 103	n = 60	n = 20		
"My medication review was done without having to be requested."	142 (38.1)	99 (52.1)	10 (9.7)	25 (41.7)	8 (40.0)	0.002	
Patient answered yes to: "Were you told to stop using any of your prescription medications?"	61 (16.4)	41 (21.6)	8 (7.8)	9 (15.0)	3 (15.0)	0.024	Most common drug classes: antidiabetics (n = 12), antilipidemics (n = 7), renin-angiotensin-aldosterone system inhibitors (n = 7), NSAIDs (n = 7)
Patient answered yes to "Were you told to change the dosage of any prescription medications?"	77 (20.6)	52 (27.4)	7 (6.8)	15 (25.0)	3 (15.0)	<0.001	Most common drug classes: antidiabetics (n = 15), diuretics (n = 10), anticoagulants (n = 7), antilipidemics (n = 7), beta-adrenergic blocking agents (n = 6)
Patient answered yes to "Were you told to stop or reduce use of any nonprescription medications, vitamins, or herbal remedies?"	23 (6.2)	10 (5.3)	5 (4.9)	8 (13.3)	0 (0.0)	0.065	Most common OTCs/herbals: NSAIDs (n = 13), vitamins (n = 7), calcium (n = 2), potassium (n = 1), omeprazole (n = 1), glucosamine (n = 1)
Patient answered yes to "Were you told to avoid certain foods or drinks when taking one or more of your medications?"	105 (28.2)	53 (27.9)	26 (25.2)	23 (38.3)	3 (15.0)	0.156	Most common food/drinks: citrus and cranberry products (n = 28), alcohol (n = 14), dark green vegetables (n = 10), high-sugar foods (n = 8), dairy (n = 4), caffeine (n = 1)
Patient answered yes to "Were you told that one or more of your medications were available at a lower cost to you?"	56 (15.0)	29 (15.3)	16 (15.5)	10 (16.7)	1 (5.0)	0.630	Most common cost-savings: availability of generic therapeutic substitutes (n = 19), available at military pharmacy (n = 6), by mail order (n = 4)
Patient answered yes to "Did your pharmacist or doctor discover any medications that he or she did not know you were taking?"	22 (5.9)	9 (4.7)	10 (9.7)	3 (5.0)	0 (0.0)	0.213	Most common drug classes: antiulcer agents and acid suppressants (n = 4), antidiabetic agents (n = 3), genitourinary smooth muscle relaxants (n = 3)
Patient answered yes to "Do you feel that this medication review was worth doing?"	317 (85.0)	162 (85.3)	93 (90.3)	51 (85.0)	11 (55.0)	0.001	Most common reasons: confirmed safety of drug regimen (n = 92), better understood their drug regimen (n = 23)

^aA total of 42, 18, and 45 respondents obtained reviews at a military pharmacy, mail order pharmacy, and community pharmacy, respectively; some respondents sought reviews at multiple pharmacies. The mail order pharmacy conducted all medication reviews by telephone.

^bA total of 21, 14, and 36 respondents obtained reviews at a military pharmacy, mail order pharmacy, and community pharmacy, respectively; some respondents sought reviews at multiple pharmacies. The mail order pharmacy conducted all medication reviews by telephone.

^cOther locations reported included medical centers and self-review.

^dStatistical significance assessed using Pearson chi-square tests.

NSAID = nonsteroidal anti-inflammatory drug; OTC = over-the-counter; PIP = polypharmacy intervention pilot.

whose review was conducted at the physician's office, the pharmacy, or both perceived the medication review to be valuable. No significant differences across review locations were observed among gender, age group, rank, enrollment status, or catchment status (tabular data not shown).

During the 90-day baseline period, subjects who received a PIP invitation (n = 3,249 with complete data; Figure 2) and comparison group subjects (n = 3,260 with complete data) used a mean (SD) of 15.26 (3.60) and 14.71 (3.68) medications, respectively (Table 5). These medication counts declined in the post-intervention period in both groups, to a mean (SD) of 14.10 (4.40) for PIP subjects and 13.51 (4.38) for the comparison group (P = 0.767). Similar findings were observed for main-

tenance medications, including mean (SD) declines from 12.36 (2.03) to 11.10 (3.11) for PIP subjects and from 11.80 (1.95) to 10.59 (3.01) for comparison group subjects (P = 0.488).

Among PIP subjects who completed the medication review and returned a survey (n = 337 with complete data) and their matched counterparts (n = 318 with complete data), results were similar; total medication counts declined from a mean (SD) of 14.73 (3.18) to 13.61 (3.74) in those completing the PIP and from 14.13 (3.39) to 13.16 (4.09) in the comparison group (P = 0.608). Mean (SD) declines in number of maintenance drugs, 1.07 (2.50) in the PIP group and 1.12 (2.68) in the comparison group, also did not significantly differ (P = 0.812).

Change in frequency of DDIs in the medication lists did

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TABLE 5 Prescription Drug Utilization Measures for PIP Versus Comparison Group Subjects

PIP ^a						Comparison Group ^a							
All Subjects													
Change in prescription drug utilization ^b	Baseline ^c		Post-Intervention ^c		Mean Change		Baseline ^c		Post-Intervention ^c		Mean Change		P Value ^d
Surviving subjects - n	3,249						3,260						
Mean [SD] number of prescription drugs ^b													
Total for all drugs	15.26	[3.60]	14.10	[4.40]	-1.17	[4.02]	14.71	[3.68]	13.51	[4.38]	-1.19	[3.92]	0.767
Maintenance drugs	12.36	[2.03]	11.10	[3.11]	-1.26	[2.87]	11.80	[1.95]	10.59	[3.01]	-1.21	[2.83]	0.488
Beers list drugs ^{b,e}													
High risk	0.49	[0.76]	0.48	[0.75]	0.00	[0.65]	0.49	[0.76]	0.44	[0.72]	-0.05	[0.66]	0.033
Low risk	0.41	[0.61]	0.40	[0.60]	-0.02	[0.44]	0.42	[0.63]	0.38	[0.60]	-0.04	[0.45]	0.061
Severity level 1 DDIs	0.08	[0.34]	0.08	[0.32]	0.00	[0.33]	0.07	[0.31]	0.06	[0.30]	0.00	[0.32]	0.910
Therapeutic category ^f													
40:00 - Electrolytic, caloric, and water balance	1.06	[0.91]	0.99	[0.88]	-0.06	[0.67]	1.03	[0.90]	0.93	[0.86]	-0.10	[0.60]	0.038
Disease states ^g													
Hypertension	2.35	[1.17]	2.21	[1.12]	-0.14	[0.84]	2.36	[1.20]	2.17	[1.12]	-0.18	[0.83]	0.028
Case Subjects Completing Study and Matched Comparison Subjects													
Surviving subjects - n	337						318						
Mean [SD] number of prescription drugs ^b													
Total for all drugs	14.73	[3.18]	13.61	[3.74]	-1.12	[3.57]	14.13	[3.39]	13.16	[4.09]	-0.97	[3.75]	0.608
Maintenance drugs	12.20	[1.93]	11.13	[2.80]	-1.07	[2.50]	11.61	[1.83]	10.49	[2.90]	-1.12	[2.68]	0.812
Beers list drugs ^{b,e}													
High risk	0.40	[0.67]	0.43	[0.69]	0.03	[0.59]	0.38	[0.62]	0.34	[0.59]	-0.05	[0.57]	0.159
Low risk	0.38	[0.62]	0.37	[0.60]	0.00	[0.42]	0.42	[0.61]	0.40	[0.62]	-0.03	[0.45]	0.584
Severity level 1 DDIs	0.10	[0.38]	0.07	[0.03]	-0.03	[0.25]	0.05	[0.25]	0.03	[0.18]	-0.02	[0.24]	0.575
Therapeutic category ^f													
40:00 - Electrolytic, caloric, and water balance	1.00	[0.82]	0.91	[0.83]	-0.09	[0.58]	0.92	[0.85]	0.80	[0.79]	-0.12	[0.58]	0.684
Disease states ^g													
Hypertension	2.36	[1.15]	2.25	[1.13]	-0.11	[0.79]	2.31	[1.14]	2.21	[1.10]	-0.10	[0.75]	0.882

^aExcludes 1,203 (all study subjects) and 91 (subjects completing study) who were confirmed dead or hospitalized during the post-intervention period using DoD administrative data. Comparison group subjects were matched on propensity scores and demographic characteristics.

^bA prescription medication was defined by 1 or more fills for a unique GCN during a 90-day period.

^cEach time period was 90 days long. The baseline period began on May 3, 2008, and ended on July 31, 2008. The post-intervention period began on the survey return date for case subjects completing the study and on December 1, 2008, for case subjects not completing the study. For a comparison group subject, the post-intervention period was that of his or her matched case subject.

^dStatistical significance assessed the between-group differences in pre-intervention to post-intervention change using a 2-sided t test.

^eOnly subjects aged 65 years or older (2,426 study cases with 2,436 comparison subjects and 240 cases that completed the study with 259 comparison subjects) were assessed for presence of 1 or more Beers list medications in their baseline medication lists.

^fNo statistically significant differences ($P < 0.05$) were observed for any other 2-digit AHFS therapeutic category.

^gNo statistically significant differences ($P < 0.05$) were observed for other disease states examined including cystic fibrosis, end-stage renal disease, human immunodeficiency virus, anxiety and tension, respiratory illness, bipolar disorder, cardiac disease, coronary peripheral artery disease, depression, diabetes, epilepsy, acid peptic disease, glaucoma, gout, hyperlipidemia, Crohn's disease and ulcerative colitis, liver failure, malignancies, pain, pain and inflammation, Parkinson's disease, psychotic illness, renal disease, rheumatologic conditions, thyroid disorder, transplants, or tuberculosis.

AHFS=American Hospital Formulary Service; DDI=drug-drug interaction; DoD=Department of Defense; GCN=generic code number; PIP=polypharmacy intervention program; SD=standard deviation.

not significantly differ by study group, in the analyses both of all study cases ($P=0.910$) or of those completing a medication review and returning the survey ($P=0.575$). Comparing the subjects who received a PIP invitation with their matched counterparts, small but statistically significant differences were observed for several measures, including use of high-risk Beers list medications ($P=0.033$); use of electrolytic, caloric, and water balance medications ($P=0.038$); and use of medications

to treat hypertension ($P=0.028$). However, for all 3 of these measures, the magnitude of the decrease observed among comparison subjects exceeded that observed among the cases, and none of these comparisons was statistically significant for the subgroup of those completing the study relative to their matched counterparts. All other therapeutic categories and disease states examined yielded no statistically significant differences between case and comparison subjects.

A post-hoc statistical power calculation using the Student's *t*-test with an alpha of 0.05 and an effect size (Cohen's *d*) of 0.2 yielded 100% statistical power to detect differences in the mean numbers of medications between the 3,249 case and 3,260 comparison subjects. The same calculation performed for the 337 case subjects completing the study and their 318 comparison subjects yielded a power of 72.5%. We also compared mean differences in prescription medication utilization between smaller subgroups, specifically among those that reported stopping a medication on their surveys (*n*=52, after removing case subjects for whom post-intervention data were not complete) relative to their matched comparison subjects (*n*=53), as well as those who reported a medication review in a doctor's office (*n*=190) versus a pharmacy (*n*=103). While no differences were significant, the small cell size further reduced statistical power and our ability to make meaningful comparisons.

■ Discussion

The first PIP study objective was to determine if beneficiaries would respond to an intervention letter and seek a medication review if one had not recently occurred. Our study findings on this point are inconclusive. Only 404 of 1,469 respondents to the consent letter declined participation on the basis of a recent medication review, but 38% of the study completers indicated that their reviews were performed without a request, suggesting that medication reviews are already part of their routine care. Little may be assumed regarding the 2,387 subjects who did not respond to the consent letter or the 233 subjects who withdrew from the study. However, it is possible that some of these patients were motivated by the initial consent letter to request a medication review during their next visit to the physician or pharmacist, without actively participating in or completing the study, a notion consistent with the Hawthorne effect.¹⁸ For this reason, utilization analyses were performed for all those who received the consent letter, as well as for those who completed the study.

Another PIP objective was to determine if a significant change in medication utilization occurred after a medication review. Among the subjects who completed the study, as well as those who reported a change in their medication regimens, no statistically significant changes following the medication review were observed relative to their matched comparison subjects with respect to the number or classes of medications used, the use of contraindicated drug combinations, or Beers list drugs. Small statistically significant utilization differences observed on a few measures when comparing all those who received a PIP invitation with their matched counterparts may be due to differences among health care practices in NC relative to the states from which the comparison population was drawn or possibly to multiple comparisons (i.e., cumulative type 1 error). The overall decrease in mean prescription utilization observed for both cases and comparison subjects

was likely partially attributable to regression to the mean and may also have been attributable to unintended inclusion of subjects who died, were hospitalized, or otherwise did not use their TRICARE drug benefit throughout the post-intervention period, thereby artificially lowering the mean utilization rates. Hospitalizations and deaths are not readily detectable in the DoD administrative data unless they occur at a military hospital or civilian hospital within the TRICARE network.

Polypharmacy interventions focused on patients who use many prescription medications generally result in a reduction in the number of medications, the number of high-risk drugs, or drug combinations in a patient's regimen,^{6,7,19} but polypharmacy has also been associated with underuse of medications.²⁰ The absence of significant changes following the medication review in the present study suggests that either the methodology was not sensitive enough to detect the changes; the medication regimens for study subjects were already optimized to the extent obtainable through a routine medication review; or medication reviews are not an effective means of resolving polypharmacy-related risk in a patient population with many comorbidities and highly complex drug regimens, such as the present study sample.

A common theme reiterated by respondents who completed the survey was "my doctor knows what I am taking." Undoubtedly, discussion of a patient's medication use occurs during most health care visits. However, a provider's awareness of a patient's medication regimen may not lead to optimization. Most of the changes in the drug regimen observed in the present study appeared to focus on dosage adjustments for currently used medications or substitution within the same therapeutic class. This finding suggests that tweaking of prescription regimens is common, but provides little evidence that a critical assessment of all the medications in use was performed.

The anecdotal evidence that older patients frequently use herbal medications, coupled with the conspicuous absence of herbal remedies from the medications that subjects were told to stop using, also suggests that providers may not have adequate awareness of all nonprescription agents in use. Patients may not report herbal remedy use to their physician if they do not think of these products as medications. A survey of primary care physicians revealed that less than 50% document or review use of herbal or other alternative treatments when performing a medication review.²¹ The National Committee for Quality Assurance physician metric for medication review among older adults, introduced in 2009, specifies that the complete medication list, including OTC and herbal therapies, and the date of the annual medication review be documented in the patient medical record.²² While "counseling about medication" is also specified, the metric provides no guidance regarding how reviews should be conducted, and it is likely that the tools, methods, and rigor applied vary widely. A content analysis of transcripts from routine physician-conducted medication reviews with patients aged 65 years or older found that

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mention by name of all medications in use occurred in 54% of visits; however, a systematic discussion that touched on at least 1 medication management topic for each medication occurred in only 28% of visits, with efficacy and directions most commonly discussed for each. A comprehensive evaluation, including discussion of dosing, adherence, efficacy, and side effects of all chronic medications in use, did not occur in any of the 100 visits studied.²³

The relatively high utilization of Beers list medications by approximately one-third of both cases and comparison subjects aged 65 years or older reinforces the notion that avoidance of these medications has not been widely assimilated into prescribing practice for the elderly.¹⁹ However, the merits of compliance with the Beers list as a measure of prescribing quality have been called into question. Evidence supporting the increased prevalence of adverse outcomes with use of Beers list medications is mixed.²⁴⁻²⁶ Among most commonly observed, high-risk Beers list medications in our study, only promethazine, cyclobenzaprine, and diazepam are also included in the 2006 Health Plan Employer Data and Information Set list of potentially inappropriate medications for the elderly.²⁶ It is noteworthy that 31% of the DDI pairs observed among those aged 65 years or older in the present study sample included a Beers list medication considered to be high risk, most commonly oxybutynin, dicyclomine, and hysocyamine. No medications included in the observed DDI pairs included a low-risk Beers list medication.

Among the 7% of the study sample with 1 or more severity level 1 DDI in their baseline medication list, more than 70% of the medication pairs included oral, solid formulations of potassium chloride. Solid formulations of potassium chloride are considered contraindicated in patients receiving agents with anticholinergic properties at sufficient doses to exert anticholinergic effects. Concomitant use of these medications may arrest or delay passage of the potassium chloride tablet through the gastrointestinal (GI) tract, potentially resulting in upper GI bleeding and small bowel ulceration, stenosis, perforation, and obstruction.²⁷ For a prescription that generates an interaction alert to be covered under TRICARE, the dispensing pharmacist must override the alert. It is unclear if the overrides for patients in the present study were a result of a case-by-case assessment of the risk to patient safety or a general alert-fatigue response, an increasingly recognized problem in electronic alerting systems for prescription drugs.²⁸

The extent to which interaction alerts are communicated to the prescriber by the dispensing pharmacist is not known. It is possible that pharmacists or prescribers either do not recognize these interaction risks as significant or believe the benefits of each medication outweigh the potential risk. This finding suggests that automated alerts involving solid formulation of potassium chloride should be refined to focus on the DDI pairs that pose the most serious risk to the patient's overall well-being. However, it is possible that some patients did not

take potentially interacting medications concomitantly. The frequency with which patients received specific instructions to minimize interaction risk or whether liquid formulations of potassium chloride were considered is not known. While a high prevalence of possible DDIs involving potassium preparations have been reported elsewhere, the interaction risk was recognized as less than severe.²⁹

Though not readily apparent in this study, there is evidence that pharmacist involvement in the medication review process results in greater coverage of medications reviewed and more interventions than if a pharmacist were not involved, without evidence of negative outcomes.³⁰ However, most of the randomized trials examining the impact of pharmacist interventions focused on disease-specific medication use. Although pharmacist-led interventions are generally not associated with reduced mortality or hospital admission rates in meta-analyses,^{31,32} improvements in medication adherence, persistence, and systolic blood pressure have been observed in randomized trials of cardiac patient-centered interventions by trained pharmacists.³³⁻³⁵ Improvements were found to dissipate, however, when the intervention was discontinued.³³⁻³⁵ Improved glycosylated hemoglobin (A1c) levels have also been associated with active pharmacist interventions, particularly if the pharmacist is afforded prescriptive authority.³⁶

Over one-half of PIP study participants bypassed the pharmacy and sought drug reviews at their physician's office. This finding represents a missed opportunity for pharmacists to actively participate in the review process. It is not clear the extent to which patients recognize that pharmacy services range beyond medication dispensing.^{37,38} In particular, elderly patients have been reported to actively resist unsolicited advice rendered by pharmacists.³⁹ Prescriber reaction to pharmacist-provided medication reconciliation is also mixed.⁴⁰ Closer pharmacist-patient relations are the cornerstone of Medication Therapy Management (MTM) programs currently being mandated by the Centers for Medicare & Medicaid Services (CMS), and a significant marketing effort may be required to educate both patients and prescribers on the expertise that pharmacists can contribute. Likewise, community pharmacies and other MTM providers must provide necessary resources for their pharmacists to provide MTM services when called on to do so. Prior surveys of pharmacists found that most believed MTM was valuable and felt comfortable providing the service but felt they were constrained by inadequate time and staffing.⁴¹⁻⁴³ Absence of reimbursement for the extra time spent providing MTM services was cited frequently as a problem among pharmacists who were providing MTM without compensation and those who desired to initiate an MTM program.⁴¹⁻⁴³

Limitations

Several limitations must be considered when interpreting our findings. First, the 9.7% completion rate for the study greatly limited our statistical power to compare medication utilization

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before and after the intervention among subjects who completed the study and may have limited the subsample of those who completed the study to a highly motivated or otherwise nonrepresentative group. Second, the pilot study protocol included the preliminary step of gaining informed consent before sending the intervention package to participating subjects. This step may have discouraged less healthy beneficiaries from participating and introduced a longer fielding period with increased subject attrition due to death, illness, or hospitalization. Third, the 90-day baseline and post-intervention periods may have been inadequate for capturing changes in medication usage. Subjects may also have died or been institutionalized without our knowledge or obtained additional medications outside the 90-day study period or through a pathway not captured in our dataset.

Fourth, pharmacy fill data permit examination of only dispensed prescription medications, which may differ from actual medication consumption by beneficiaries. Our use of GCN-based medication counting may have overestimated the number of medications used because changes in dosage of the same drug and therapeutically similar drugs of different formulations would be counted as multiple medications, even if the medications were used sequentially rather than simultaneously during the 90-day baseline period. Fifth, adherence to their medication regimen and the extent to which beneficiaries were using their medications concurrently are potentially important considerations that cannot be addressed using fill records alone. These limitations are mitigated to some degree by comparison of the intervention group with a matched comparison group. However, small changes in use of prescription or OTC medication, diet, other clinically relevant adjustments to medication usage resulting from the intervention, or important changes in subjects' health status during the intervention were not detectable using our methodology. Differences in health care practice in NC, relative to the neighboring states from which the comparison subjects were selected, may have confounded our study and limited our ability to generalize the findings.

Sixth, providing more specific instructions or templates for conducting the medication review would be prudent, particularly to ensure that OTC products and herbal medications are discussed. A feedback mechanism that lets the researcher know whether the medication review was performed according to the instructions provided would also be helpful. Seventh, additional measures of medication utilization should also be considered. Including a measure of past medication adherence for critical medications—for propensity-matching of cases to comparison subjects and as a study outcome—may also yield more meaningful results.

Conclusions

This study examined the feasibility of using mailed correspondence to promote patient-initiated medication reviews among TRICARE beneficiaries who obtained 10 or more

maintenance medications within a 90-day baseline period. We found that the rate of response to the mailing was low. Additionally, medication reviews, although viewed positively by most patients, yielded no significant change in prescription medication utilization. Whether the medication regimens for these patients are already optimized requires further investigation. DoD desires to gain greater assurance that medication use is being actively managed, particularly among those who use multiple prescription medications. Additional pilot studies to incorporate pharmacist-based services into the TRICARE benefit, consistent with MTM principles set forth by CMS, are currently being studied.

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DISCLOSURES

All authors of this manuscript are employed solely by the Department of Defense and hold no affiliation with organizations that may incur a financial benefit as a result of this work being published.

Concept and design were primarily the responsibility of Bacon and McGinnis, with the assistance of Linton. Cottrell and Linton together performed the data collection, with other authors contributing. Data interpretation was performed by Bacon, Devine, Linton, and Trice. The manuscript was written primarily by Linton and revised primarily by Linton and McAllister.

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DISCLAIMER

The thoughts and opinions expressed in this paper are those of the authors and do not necessarily represent the official policy or position of the U.S. Department of Defense.

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